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# Occupational and Leisure-Time Physical Activity and Risk of Colon Cancer by Subsite

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## Learning Objectives

- Identify a plausible mechanism or mechanisms by which the level of physical exercise—at work and at leisure—might influence the risk of colon cancer.
- Describe the extent to which, in this population-based case-control study, reported levels of leisure-time and occupational exercise were associated with the risk of cancer developing in the colon as a whole and in different parts of the colon.
- Point out whether and how any relationship between the level of physical activity and the risk of colon cancer may be altered by the body mass index.

## Abstract

**Objective:** Studies of physical activity and colon cancer risk by anatomic site have provided inconsistent results. **Methods:** We analyzed data from a population-based case-control study conducted in Iowa involving 685 colon cancer cases and 2434 control subjects. **Results:** Among those who reported recreational activity more than twice per week, a 30% risk reduction of colon cancer was observed for all sites with a 40% risk reduction for cancer of the right colon. Occupational physical activity was also associated with a reduced risk of colon cancer. The risk was the lowest for those with both high occupational and recreational physical activity (odds ratio, 0.5; 95% confidence interval, 0.3–0.8). **Conclusions:** Increased physical activity was inversely associated with colon cancer risk. The inverse associations were stronger for the right than for the left colon. (J Occup Environ Med. 2006;48:236–243)

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An inverse association between physical activity and colon cancer risk has been consistently reported by previous epidemiologic studies, whereas associations between physical activity and colon cancer risk by anatomic site have been inconclusive.<sup>1</sup> Some studies found essentially no effect of physical activity on the risk of cancer of the right colon.<sup>1–8</sup> Other studies, however, found the association was the greatest for the right colon,<sup>9,10</sup> whereas a few others found no obvious risk pattern by anatomic subsite.<sup>11–14</sup> An inverse relationship between physical activity and colon cancer risk is biologically plausible. It has been suggested that increased physical activity increases gut motility and decreases fecal transit time. A shortened intestinal transit time could reduce the risk of colon cancer by decreasing the amount of contact between potential carcinogens in the fecal stream and the colonic mucosa.<sup>15</sup> Several other hypotheses, including the physiological effect on fat metabolism or hormonal changes from physical exercise, appear to be more speculative.<sup>16–20</sup>

Although a number of studies have investigated the association between physical activity and colon cancer risk, few have examined the joint effect of recreational and occupational physical activity. A recent study by Colbert et al<sup>1</sup> reported an almost 70% risk reduction among those most active in both work and leisure settings. Studies by Gerhardsson et al<sup>21</sup> and Longnecker et al<sup>22</sup> also found that risk was lowest among those with elevated physical activity during both occupational and recreational hours.

To further examine the relationship between recreational and occupational physical activity and risk of colon cancer by anatomic site, and to evaluate their joint effect on the risk of colon cancer, we analyzed data from a population-based case-control study conducted in the state of Iowa.

## Materials and Methods

### Study Population

Detailed information regarding the study design is described elsewhere.<sup>23</sup> Briefly, a total of 801 histologically confirmed incident colon cancer cases, aged 40 to 85, were identified by the State Health Registry of Iowa in March through December, 1987. Eligible cases were residents of Iowa and were without a previous diagnosis of a malignant neoplasm, except for non-melanoma skin cancer. Of the 801 newly diagnosed subjects, 685 (86%) colon cancer cases participated in the study (347 males and 338 females). Colon cancer was part of a larger study that also included cancers of the brain, kidney, pancreas, bladder, and rectum.

A total of 2434 (1601 males and 833 females) population-based control subjects were frequency-matched by sex and 5-year age groups to all cases in the larger study in the years 1986 through 1989. The matching ratio for colon cancer cases was approximately 3.6:1. Control subjects under age 65 were randomly selected from computerized state driver's license records. Control subjects aged 65 years and older were selected from U.S. Health Care Financing Administration listings. Like with the cases, persons with a previous cancer diagnosis, except for nonmelanoma skin cancer, were excluded from consideration as control subjects. The participation rate was 82% for control subjects younger than 65 and 79% for those aged 65 and older.

### Data Collection

After obtaining physician consent for cases, subjects were first contacted by mail and then by telephone.

Subjects reluctant to participate were provided the option of responding to an abbreviated telephone questionnaire that did not include leisure time physical activity and detailed occupational history questions. The 100 cases and 262 control subjects who responded in this manner were excluded from the analysis. A total of 585 cases and 2172 control subjects completed a postal questionnaire, which was used to collect detailed information on leisure-time physical activity and other exposures (such as demographic factors, residential and smoking histories, frequency of dietary intakes, medical history, first-degree family history of cancer). For leisure-time physical activity, respondents were asked to report their usual nonoccupational exercise activities in one of four categories. Specifically, the participants were asked: "During most of your adult life, how often did you usually do strenuous or moderate exercise such as jogging, swimming laps, gardening, or walking briskly for 10 minutes?" Subjects were asked not to include physical activities connected with any jobs they may have held. The response categories were: one time per day or more, two to six times per week, one to four times per month, and less than once a month or never.

Detailed information on lifetime occupational history was collected from 420 cases and 1669 control subjects. Respondents were asked to report all jobs they held for 5 years or longer since age 16. For each job reported, subjects were asked for the job title, type of business or industry, the year when they began and ended each job, and the activities or duties associated with each job. Job titles and industries from occupational histories were subsequently coded according to the Standard Industry Classification (SIC)<sup>24</sup> and the Standard Occupational Classification Manual (SOC)<sup>25</sup> codes. Assignment of occupational physical activity into one of three levels was based on occupations held by the subjects. We

calculated the occupational physical activity levels 10 years, 20 years, and 30 years before disease diagnosis or interview as done by Longnecker et al.<sup>22</sup> Subjects with low occupational physical activity for all three time periods (10, 20, and 30 years ago) were compared with those who were most active in all three periods or compared with remaining subjects. We also calculated occupational physical activity levels at age 20, age 30, and age 40, and compared subjects who had low occupational physical activity for all three ages with those who were most active in all three age groups or compared with the remaining subjects. The occupational activity levels at all three ages (ages 20, 30, and 40) or at all three time periods (10, 20, and 30 years ago) could be regarded as measures of cumulative lifetime occupational physical activity.

An occupational physical activity index was also created for each subject based on the activity level associated with the job that required the highest physical activity for that person. We defined occupational physical activity based on the methods by Vetter et al<sup>26</sup> and Dosemeci et al.<sup>27</sup> An occupation was considered to require high physical activity if it involved physical activity more than 80% of the time, moderate physical activity if it involved physical activity 20% to 80% of the time, or low activity if it involved physical activity less than 20% of the time.

Intake of selected nutrients, evaluated in our data analyses as potential confounders, was computed on the basis of a subject's frequency of consumption of each of 55 food items and the nutrient content of an average serving. The nutrient content of an average serving was based on sex-specific portion sizes and food composition data obtained from the National Health and Nutrition Examination Survey (NHANES II) nutrient database.<sup>28</sup> For each macronutrient, consumption categories were created by dividing the frequency distribution of consumption

of the control group into approximate sex-specific quartiles. When consumption level of a macronutrient was unknown, it was given a discrete "unknown" value.

## Data Analysis

Risks for colon cancer overall or by anatomic subsite associated with occupational or leisure-time physical activity were calculated using unconditional logistic regression models. Odds ratios (ORs) and 95% confidence intervals (95% CIs) were calculated using SAS statistical software (SAS Institute, Inc., Cary, NC). Left colon cancer cases included descending colon (50 cases), sigmoid colon (262 cases), and the splenic flexure of the colon (29 cases). Right colon cancer cases included ascending colon (88 cases), cecum (146 cases), and the hepatic flexure of the colon (34 cases). Fifty-eight subjects were diagnosed with cancer of the transverse colon. Seventeen others could not be assigned to a subsite, and one involved the appendix. Although it was not feasible to analyze the data for these cancers separately, we included these subjects when all sites were considered.

The following potential confounders, which showed an impact on the observed ORs, were included in the final regression models: level of education ( $\leq 8$ , 9–11, 12–15,  $\geq 16$  years), first-degree relative with colon cancer (yes/no), dietary fat intake (by quartiles), and fiber intake (by quartiles). The age distribution of cases and control subjects was similar. However, because age is associated with both colon cancer risk and physical activity, we included age in the final model to control for possible residual confounding (40–54, 55–64, 65–74, 75–85 years). Additional adjustment for body mass index (BMI), population size in reported places of residence (based on 1980 census) averaged over a lifetime, cigarette smoking, and for other types of cancer in a first-degree relative did not result in a material change to the observed associations; thus, these vari-

ables were not included in the final models.

The joint effect between leisure-time physical activity and occupational physical activity was evaluated, and ORs were calculated relative to those who required low physical activity at work and who exercised less than once per month. The joint effect between physical activity and BMI was evaluated by including a product term in the logistic regression model. Categorical variables of BMI and physical activity were used to evaluate the statistical significance of the interactions under the multiplicative model by the Wald  $\chi^2$  test.

## Results

Among males, 17% of the cases and 5.4% of the control subjects reported having one or more first-degree relatives with colon cancer; among females, the corresponding

proportions were 16% for cases and 6.8% for control subjects (Table 1). Cases also had higher BMI and lower dietary fiber intakes than control subjects. Among males, cases reported higher saturated fat intakes. No other selected factors showed a major difference between the cases and control subjects.

Elevated leisure-time physical activity was associated with a significantly reduced risk of colon cancer (Table 2). Overall, there was a 30% (OR, 0.7; 95% CI = 0.6–0.9) reduction in risk of colon cancer for those who reported moderate/strenuous recreational exercise more than twice per week. For cancer of the right colon, significant risk reductions of 50% among males (OR, 0.5; 95% CI = 0.3–0.9) and 40% among females (OR, 0.6; 95% CI = 0.4–0.9) were observed for those who reported moderate/strenuous recre-

**TABLE 1**

Number and Proportion (%) of Colon Cancer Cases and Control Subjects Based on Selected Characteristics in a Case-Control Study of Colon Cancer in Iowa

Factor	Men		Women	
	Cases (%)	Controls (%)	Cases (%)	Controls (%)
Age				
40–64	102 (29.4)	507 (31.7)	104 (30.8)	283 (34.0)
65–74	141 (40.6)	629 (39.3)	123 (36.4)	276 (33.1)
75–85	104 (30.0)	465 (29.0)	111 (32.8)	274 (32.9)
First-degree relative with colon cancer				
No	258 (74.3)	1431 (89.4)	261 (77.2)	743 (89.2)
Yes	59 (17.0)	87 (5.4)	54 (16.0)	57 (6.8)
Unknown	30 (8.7)	83 (5.2)	23 (6.8)	33 (4.0)
Body mass index (kg/m <sup>2</sup> )				
<23.5	69 (19.9)	402 (25.1)	117 (34.6)	322 (38.7)
23.5–26.3	114 (32.8)	546 (34.1)	73 (21.6)	191 (22.9)
>26.3	127 (36.6)	544 (34.0)	104 (30.8)	230 (27.6)
Unknown	37 (10.7)	109 (6.8)	44 (13.0)	90 (10.8)
Fiber				
Quartile 1	72 (20.7)	312 (19.5)	85 (25.2)	160 (19.2)
Quartile 2	79 (22.8)	312 (19.5)	67 (19.8)	160 (19.2)
Quartile 3	57 (16.4)	311 (19.4)	53 (15.7)	159 (19.1)
Quartile 4	61 (17.6)	312 (19.5)	42 (12.4)	160 (19.2)
Unknown	78 (22.5)	354 (22.1)	91 (26.9)	194 (23.3)
Saturated fat				
Quartile 1	54 (15.6)	312 (19.5)	66 (19.5)	160 (19.2)
Quartile 2	64 (18.4)	313 (19.5)	54 (16.0)	160 (19.2)
Quartile 3	70 (20.2)	310 (19.4)	67 (19.8)	159 (19.1)
Quartile 4	81 (23.3)	312 (19.5)	60 (17.8)	160 (19.2)
Unknown	78 (22.5)	354 (22.1)	91 (26.9)	194 (23.3)

**TABLE 2**

Leisure-Time Physical Activity and Risk of Colon Cancer by Gender and Anatomic Subsite

Moderate/Strenuous Leisure-Time Physical Activity†	All Sites		Right Colon*		Left Colon*	
	Ca/Co‡	OR§ (95% CI)	Ca/Co‡	OR§ (95% CI)	Ca/Co‡	OR§ (95% CI)
Males and females						
<1/mo	237/732	1.0	100/732	1.0	112/732	1.0
1–4/mo	86/348	0.7 (0.5–1.0)	35/348	0.7 (0.5–1.1)	44/348	0.7 (0.5–1.1)
≥2/wk	262/1092	0.7 (0.6–0.9)	90/1092	0.6 (0.4–0.8)	136/1092	0.8 (0.6–1.1)
P for trend		0.05		0.003		0.53
Males¶						
<1/mo	137/553	1.0	52/553	1.0	72/553	1.0
1–4/mo	45/216	0.9 (0.6–1.3)	17/216	0.9 (0.5–1.7)	25/216	0.9 (0.5–1.5)
≥2/wk	117/683	0.7 (0.5–1.0)	33/683	0.5 (0.3–0.9)	70/683	0.8 (0.6–1.2)
P for trend		0.12		0.02		0.55
Females^						
<1/mo	100/179	1.0	48/179	1.0	40/179	1.0
1–4/mo	41/132	0.6 (0.4–0.9)	18/132	0.5 (0.3–1.0)	19/132	0.6 (0.3–1.1)
≥2/wk	145/409	0.7 (0.5–1.0)	57/409	0.6 (0.4–0.9)	66/409	0.8 (0.5–1.2)
P for trend		0.11		0.02		0.62

\*Right colon = cecum, ascending colon, and hepatic flexure; left colon = splenic flexure, descending colon, and sigmoid colon.

†One hundred cases and 262 control subjects did not provide this information.

‡Number of cases and control subjects.

§Adjusted for age, gender, level of education, dietary intake of fat and fiber, and first-degree relative with colon cancer.

¶Not adjusting for gender.

OR indicates odds ratio; CI, confidence interval.

ational activity more than twice per week. For cancer of the left colon, there was a suggestion of a 10% to 30% risk reduction with increasing leisure-time physical activity. None of the associations found for the left colon, however, was statistically significant.

The results relating colon cancer risk to lifetime cumulative occupational physical activity are pre-

sented in Table 3. Subjects with low occupational physical activity for all three time periods (10, 20, and 30 years before diagnosis/interview) comprised one category. Subjects most active in all three comprised another, and the remaining subjects comprised a third category. Compared with subjects who had low occupational physical activity for all three time periods,

subjects who were most active in all three had an OR of 0.8 (95% CI = 0.5–1.2) for all sites combined, an OR of 0.7 (95% CI = 0.3–1.5) for right colon, and an OR of 0.9 (95% CI = 0.5–1.6) for left colon. Compared with subjects who had low occupational physical activity for all three age groups (ages 20, 30, and 40), those who were most active in all three age groups

**TABLE 3**

Occupational Physical Activity and Risk of Colon Cancer by Subsite at Different Ages or Periods

Occupational Physical Activity	All Sites		Right Colon		Left Colon	
	Ca/Co*	OR† (95% CI)	Ca/Co*	OR† (95% CI)	Ca/Co*	OR† (95% CI)
Activity levels 10 yr, 20 yr, and 30 yr before diagnosis/interview						
Low at all three periods	122/436	1.0	43/436	1.0	62/436	1.0
High at all three periods	33/157	0.8 (0.5–1.2)	10/157	0.7 (0.3–1.5)	20/157	0.9 (0.5–1.6)
Others	530/1841	0.9 (0.7–1.2)	215/1841	1.1 (0.7–1.6)	259/1841	0.9 (0.7–1.3)
Activity levels at age 20, age 30 and age 40						
Low at all three ages	81/318	1.0	24/318	1.0	47/318	1.0
High at all three ages	11/74	0.6 (0.3–1.2)	4/74	0.8 (0.3–2.4)	7/74	0.6 (0.3–1.4)
Others	593/2042	0.9 (0.7–1.2)	240/2042	1.1 (0.7–1.8)	287/2042	0.8 (0.6–1.1)

\*Number of cases and control subjects.

†Adjusted for age, gender, level of education, dietary intake of fat and fiber, and first-degree relative with colon cancer.

OR indicates odds ratio; CI, confidence interval.



TABLE 4

Occupational Physical Activity and Risk of Colon Cancer by Gender and Anatomic Site

Occupational Physical Activity*	All Sites		Right Colon		Left Colon	
	Ca/Co†	OR‡ (95% CI)	Ca/Co†	OR‡ (95% CI)	Ca/Co†	OR‡ (95% CI)
All subjects						
Low	169/582	1.0	60/582	1.0	87/582	1.0
Moderate	187/797	0.8 (0.7–1.1)	63/797	0.8 (0.6–1.2)	106/797	0.9 (0.7–1.3)
High	64/290	0.8 (0.6–1.1)	23/290	0.9 (0.5–1.5)	33/290	0.7 (0.5–1.2)
P for trend		0.09		0.38		0.23
Males§						
Low	77/336	1.0	22/336	1.0	43/336	1.0
Moderate	113/597	0.8 (0.6–1.1)	36/597	0.9 (0.5–1.6)	67/597	0.8 (0.5–1.3)
High	57/263	0.8 (0.5–1.2)	21/263	1.0 (0.5–2.1)	30/263	0.8 (0.4–1.3)
P for trend		0.23		0.95		0.34
Females§						
Low	92/246	1.0	38/246	1.0	44/246	1.0
Moderate	74/200	0.9 (0.6–1.4)	27/200	0.8 (0.5–1.4)	39/200	1.0 (0.6–1.7)
High	7/27	0.6 (0.2–1.4)	2/27	0.4 (0.1–1.7)	3/27	0.5 (0.1–1.6)
P for trend		0.25		0.24		0.45

\*Two hundred sixty-five cases and 765 controls did not provide this information.

†Number of cases and control subjects.

‡Adjusted for age, gender, level of education, dietary intake of fat and fiber, and first-degree relative with colon cancer.

§Not adjusted for gender.

OR indicates odds ratio; CI, confidence interval.

had an OR of 0.6 (95% CI = 0.3–1.2) for all sites combined, an OR of 0.8 (95% CI = 0.3–2.4) for right colon, and an OR of 0.6 (95% CI = 0.3–1.4) for left colon.

We also evaluated the association by using a single occupational physical activity index based on the job requiring the largest amount of physical activity. As shown in Table 4, there was a general trend of decreasing risk with increasing occupational physical activity. A 20% risk reduction (OR, 0.8; 95% CI = 0.6–1.1),

albeit insignificant, was observed when all sites were considered for males and females. Sex-specific analyses also suggested reduced risk, especially among females, for both right and left colon.

The joint effect of occupational and leisure-time physical activity showed a reduced risk of colon cancer associated with higher physical activity when compared with those who had both low occupational and leisure-time physical activity (Table 5). Among those with the highest

occupational physical activity, the risk of colon cancer decreased with increasing frequency of leisure-time physical activity. Among those with the highest frequency of leisure-time physical activity, colon cancer risk also generally decreased with increasing occupational physical activity. A significant 50% risk reduction (OR, 0.5; 95% CI = 0.3–0.8) was observed for those who had the highest frequency of leisure-time physical activity and highest occupational physical activity.

TABLE 5

Risk for Colon Cancer According to Recreational and Occupational Physical Activity

Occupational Physical Activity*	Moderate/Strenuous Leisure-Time Physical Activity						P for Trend§
	<1/Mo		1–4/Mo		≥2/Wk		
	Ca/Co†	OR‡ (95% CI)	Ca/Co†	OR‡ (95% CI)	Ca/Co†	OR‡ (95% CI)	
Low	50/125	1.0	24/118	0.5 (0.3–0.9)	92/327	0.8 (0.5–1.2)	0.41
Medium	79/284	0.7 (0.5–1.1)	30/119	0.7 (0.4–1.3)	70/380	0.5 (0.3–0.8)	0.04
High	29/90	0.9 (0.5–1.6)	10/45	0.6 (0.3–1.3)	24/145	0.5 (0.3–0.8)	0.06
P for trend¶		0.88		0.71		0.01	

\*Occupational physical activity was calculated based on job with the maximum physical activity.

†Number of cases and control subjects.

‡Odds ratio adjusted for age, gender, level of education, dietary intake of fat and fiber, and first-degree relative with colon cancer.

§P for trend across leisure time physical activity within each group of occupational physical activity.

¶P for trend across occupational physical activity within each group of leisure-time physical activity.

OR indicates odds ratio; CI, confidence interval.

TABLE 6

Risk for Colon Cancer According to Leisure-Time Physical Activity and Body Mass Index

Body Mass Index (kg/m <sup>2</sup> )	Moderate/Strenuous Leisure-Time Physical Activity						<i>P</i> for Trend‡
	<1/Mo		1–4/Mo		≥2/Wk		
	Ca/Co*	OR† (95% CI)	Ca/Co*	OR† (95% CI)	Ca/Co*	OR† (95% CI)	
>26.3	97/276	1.0	32/131	0.7 (0.4–1.0)	85/341	0.7 (0.5–0.9)	0.02
23.5–26.3	60/219	0.8 (0.5–1.1)	26/126	0.5 (0.3–0.8)	96/368	0.7 (0.5–1.0)	0.84
<23.5	70/229	0.7 (0.5–1.1)	26/87	0.7 (0.4–1.2)	78/375	0.5 (0.4–0.7)	0.02
<i>P</i> for trend§		0.03		0.25		0.32	

\*Number of cases and control subjects.

†Odds ratio adjusted for age, gender, level of education, dietary intake of fat and fiber, and first-degree relative with colon cancer.

‡*P* for trend across leisure-time physical activity within each group of body mass index.§*P* for trend across body mass index within each group of leisure-time physical activity.

OR indicates odds ratio; CI, confidence interval.

When we stratified BMI into tertiles, risk generally decreased with increasing leisure-time physical activity and significant trends were observed within the lowest and the highest tertiles ( $P = 0.02$ , Table 6). Compared with persons in the highest tertile of BMI ( $>26.3$  kg/m<sup>2</sup>) having minimal leisure-time physical activity, physically active ( $>2\times/\text{wk}$ ) subjects with low BMI ( $<23.5$  kg/m<sup>2</sup>) had one half the risk of colon cancer (OR, 0.5; 95% CI = 0.4–0.7). There was no significant interaction between BMI and leisure time physical activity under multiplicative model ( $P = 0.43$ ). When we stratified the analysis by sex, similar results were found for women and for men (data not shown).

## Discussion

In this population-based case-control study in Iowa, we found a significant inverse association between reported leisure-time physical activity and risk of colon cancer, with a slightly stronger association for the right colon than for the left colon in both males and females. Occupational physical activity was also associated with a reduced risk of colon cancer in this study, although results were less consistent. The joint effect of occupational and leisure-time physical activity suggested that the risk was the lowest for those with high occupational and nonoccupational physical activity.

Our results are consistent with most earlier epidemiologic studies suggesting that higher levels of leisure-time physical activity are associated with a reduced risk of colon cancer.<sup>15,29</sup> We observed an inverse association even though we used a relatively crude assessment of non-occupational physical activity based on a single question. As pointed out by others, however, a limitation of this type of assessment of leisure-time physical activity is that we were unable to address the relationship between specific activities and cancer risk, or the importance of duration of exercise or age at which a person was most active.<sup>1,15</sup>

Our study also noted a reduced risk of colon cancer associated with occupational physical activity, especially for those with high occupational activity levels at three ages we coded (20, 30, and 40 years of age) or all three periods (10, 20, and 30 years before diagnosis or interview), as measured in this study. The occupational activity levels at all three ages or at all three time periods (Table 3) could be regarded as measures of cumulative lifetime occupational physical activity. Use of lifetime occupational activity to measure the association (Table 3) seems to show a more consistent inverse association than use of a single occupational activity index (Table 4). Vena et al<sup>30</sup> also reported a strong inverse relation be-

tween higher lifetime occupational activity and the risk of colon cancer. Slattery et al<sup>31</sup> reported that different indicators of physical activity are consistently associated with a decreased risk of colon cancer. However, because people switch their jobs frequently, the use of self-reported or coded occupational physical activity data would undoubtedly result in misclassification of activity levels. It is unlikely that this misclassification differed among cases and control subjects. Such nondifferential misclassification of exposure could result in an underestimation of the association. This could partly explain the lack of a significant association between occupational physical activity and colon cancer risk in this study, especially when a single occupational physical activity index was used.

Although colon cancer risk in this study showed a less consistent association with occupational physical activity than with nonoccupational activity, we observed the lowest risk among those who reported high physical activity both at work and during leisure time. Colbert et al<sup>1</sup> recently also reported that the strongest inverse association was found among those most active in both work and leisure (relative risk, 0.3; 95% CI = 0.2–0.7). Longnecker et al<sup>22</sup> reported an OR of 0.4 (95% CI = 0.2–1.1) for those with higher physical activity in both work and

leisure. Markowitz<sup>32</sup> and Whittemore et al<sup>14</sup> also reported a joint effect of recreational and occupational physical activity on the risk of colon cancer. Unlike recent reports,<sup>33,34</sup> we did not observe a significant interaction between BMI and physical activity under the multiplicative model in this study population.

The inverse association between higher physical activity and colon cancer risk in our study was slightly stronger for the right than the left colon. Studies of physical activity and colon cancer risk by specific site have yielded inconsistent results<sup>1,15</sup> with some studies suggesting a stronger protective effect for the left colon,<sup>2-8</sup> the right colon,<sup>9,10</sup> or no difference.<sup>11-13</sup> It has been suggested that some of these discrepancies could be attributable to variation in the methods used to define anatomic subsites or to the measure of physical activity.<sup>1</sup> It could also be due to chance because the sample sizes by anatomic subsite for most of the studies, including our own, are relatively small, especially after stratification by sex.

Confounding is an unlikely explanation for the observed inverse association between physical activity and colon cancer risk. In this study, we were able to control for major colon cancer risk factors, including having a first-degree relative with colon cancer, BMI, dietary fat and fiber intakes, and level of education. Selection bias is also an unlikely explanation for the observed inverse association between physical activity and colon cancer risk. Refusal rates were low and similar between the cases and control subjects; and study participants were not informed of the hypothesis regarding physical activity and colon cancer risk.

In conclusion, our results support the hypothesis that increasing physical activity is inversely associated with colon cancer risk, with the lowest among those who had high physical activity levels at both work and leisure times. The benefits of physical activity on cardiovascular health

and other outcomes are well documented.<sup>35</sup> The growing evidence on physical activity and colon cancer risk, from this and other studies, suggests that a general increase in the level of physical activity would have additional benefits in lowering the relatively high incidence rates of this disease found in Western industrialized populations.

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